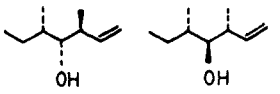
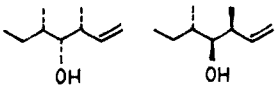
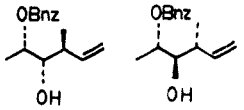
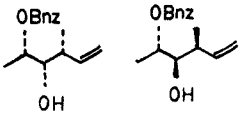
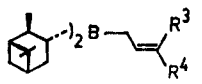
Table I. Reaction of Chiral Aldehydes 17 and 18 with the Reagents 13–16[a]

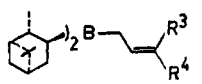
aldehydes[b]	reagents	products: yield,[c] %	products: diastereomeric ratio[d,f]
17			
	13	(75)	96:4
	14	(70)	9:91[e]
			
	15	(73)	82:18[e]
	16	(79)	4:96[e]
18			
	13	(80)	95:5
	14	(85)	3:97
			
	15	(74)	73:27
	16	(78)	1:99

[a] The reactions were carried out at −78 °C under a nitrogen atmosphere[10] by utilizing a 1:1 molar ratio of reagent to chiral aldehyde. [b] Chiral aldehydes (17, 96–97% ee; 18, 99% ee) were prepared and used in solution. The optical purity of the aldehydes were routinely checked by comparing the optical rotations of the corresponding alcohols produced by BMS reduction of the aldehydes. [c] Isolated yield. [d] The ratios of diastereomers were determined by capillary GC analysis of the product alcohols using a column of methylsilicon, 50 M × 0.25 mm. [e] In addition to the presence of the desired two diastereomers, the capillary GC analysis revealed the presence of 1–2% of the other two diastereomers, presumably arising from the presence of small amounts of the other diastereomeric reagent. [f] Configurations of the newly formed C–C bond to the configuration present in the aldehyde are predicted by analogy to the configuration realized in the products obtained in the reaction of crotyldiisopinocampheylborane derivatives with achiral aldehydes.[6a]

facial selectivities. In order to further explore the factors controlling aldehyde facial selectivity, we have examined and report herein the stereochemical features of the reactions of crotyldiisopinocampheylboranes **13–16** with aldehydes (*S*)-2-methylbutyraldehyde (**17**) and (*S*)-2-(benzyloxy)propionaldehyde (**18**).



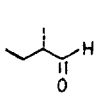
13 $R^3 = H$, $R^4 = CH_3$



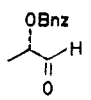
14 $R^3 = H$, $R^4 = CH_3$

15 $R^3 = CH_3$, $R^4 = H$

16 $R^3 = CH_3$, $R^4 = H$



17



18

The reagents, *B*-crotyldiisopinocampheylboranes **13–16**, are readily obtained in high stereochemical purity according to the procedure previously reported from our laboratory.[6a] All crotylboration reactions were carried out at −78 °C in ether solvent. These reactions are observed to be rapid and require less than 3 h at −78 °C. The reaction mixture was worked up by using alkaline hydrogen peroxide to remove the boron intermediate.[9] The diastereofacial selectivities of the reagents **13–16** with chiral aldehydes **17** and **18** are easily assessed by monitoring the overall diastereoselectivities achieved in the reaction. The results are summarized in Table I.

It is immediately striking that the reactions of crotylboranes **13**, **14**, and **16** with aldehydes **17** and **18** are highly stereoselective and the corresponding (3,4- and 4,5)-anti,syn, -anti,anti, and -syn,anti products have been obtained in very high facial selectivities. Even the reaction of **15** with aldehydes **17** and **18** furnished the syn,syn product in moderately good facial selectivity.

It is clear from these results that the crotyldiisopinocampheylboranes **13–16** are highly diastereoselective reagents with α-substituted chiral aldehydes **17** and **18**. The stereochemistry at the newly formed C–C bond is controlled simply by selecting the appropriate enantiomeric reagent; thus, the chirality of the reagent controls the overall diastereofacial selectivity achieved in the reaction. This synthesis is operationally very simple, providing access to all possible stereoisomers in high optical purity merely by selecting the proper antipode of the reagents and aldehydes.[11] Further, ozonification of these homoallyl alcohols should provide the corresponding aldehydes, which, on further treatment with (*E*)- or (*Z*)-crotyldiisopinocampheylboranes, would provide the homoallyl alcohols with an additional two stereocenters in high stereoselectivity. Hence, this repeating process should provide a convenient route to the numerous macrolide and polyether antibiotics.

Acknowledgment. The financial support from the National Institutes of Health (Grant GM 10937-24) is gratefully acknowledged.

(9) Alternatively, the boron intermediate can be removed by precipitation with enthanolamine. Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 2564.

(10) For techniques, see: Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, 1975; p 191.

(11) Attention is called to a recent paper[12] which describes the reaction of the (*Z*)- and (*E*)-crotylboronate with β-alkoxy-α-methylpropionaldehyde. The reaction takes the same course. In this case, it was possible to assign the structure by comparison of the spectral data for the known material.

(12) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. *J. Org. Chem.* **1987**, *52*, 316.

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Charge Reversal of Electrophilic π-Allylpalladium Intermediates: Carbonyl Allylation by Allylic Acetates with $Pd(PPh_3)_4$–Zn

Summary: Allylic acetates were reduced by zinc in the presence of a catalytic amount of $Pd(PPh_3)_4$ to serve as nucleophilic allylating agents, which reacted with aldehydes to afford the corresponding homoallylic alcohols.

Sir: Addition reaction of various allylic organometallic compounds to aldehydes has attracted notice for possible applications to stereocontrolled synthesis in the conformationally nonrigid acyclic system.[1] The allylic organo-

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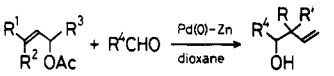
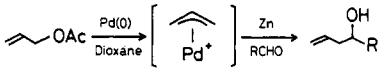
Table I. Carbonyl Allylation by Allylic Acetates with Pd(0)-Zn[a]



acetate			aldehyde		product			
R^1	R^2	R^3	R^4	time, days	R	R′	yield,[b] %	syn:anti[c]
CH_3	H	H	Ph	4	CH_3	H	71 (33)[d]	55:45
H	H	CH_3	Ph	4	CH_3	H	37[d]	53:47
CH_3	H	H	C_5H_{11}	5	CH_3	H	51	58:42
CH_3	CH_3	H	Ph	4	CH_3	CH_3	99	
Ph	H	H	Ph	5	Ph	H	70	13:87
H	H	Ph	Ph	5	Ph	H	57[d]	17:83
Ph	H	H	$CH_3CH{=}CH$	4	Ph	H	90	66:34
H	H	C_7H_{15}	Ph	4	C_7H_{15}	H	26[d]	73:27
H	H	C_7H_{15}	C_5H_{11}	6	C_7H_{15}	H	33[d]	58:42

[a] Addition reaction of allylic acetates (10 mmol) to aldehydes (2 mmol) with $Pd(PPh_3)_4$ (0.04 mmol) and Zn (10 mmol) was carried out in dioxane. [b] The yields of isolated pure products based on aldehydes. No other regioisomer was detected by 270-MHz ^1H NMR. [c] The ratio was determined by GLPC or 270-MHz ^1H NMR. [d] Two equivalents of the acetate was used.

Scheme I

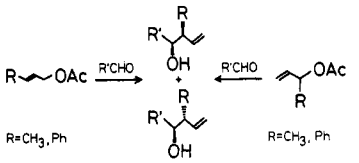


metallic compounds are generally prepared from either allylic halides[2] or olefins.[3] However, a number of these starting materials are unstable or intractable. Therefore, application of storable allylic acetates, easily derived from available allylic alcohols, as allylating agents should further enhance the usefulness of the addition reaction.[4] We report allylation of aldehydes via charge reversal of π-allylpalladium intermediates, derived from allylic acetates and palladium(0) complex, using zinc as a reducing agent (Scheme I).

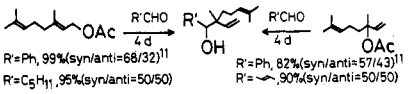
To a suspension of zinc powder (0.65 g, 10 mmol),[5] benzaldehyde (0.21 g, 2.0 mmol), and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol) in dioxane (3 mL) was added (*E*)-crotyl acetate (1.1 g, 10 mmol) dropwise for 24 h at room temperature under a nitrogen atmosphere. After being stirred for an additional 3 days at room temperature, the reaction mixture was poured into water (30 mL) and extracted with ether (2 × 25 mL). The combined extracts were dried over $MgSO_4$. Evaporation of ether and purification by column chromatography on silica gel (hexane/EtOAc, 5/1) afforded 0.23 g (71%, syn/anti = 55/45) of 2-methyl-1-phenyl-3-buten-1-ol as a colorless oil. Use of benzene, tetrahydrofuran, acetonitrile, and *N,N*-dimethylformamide as solvent inhibited the reaction dramatically compared to that for dioxane. The carbonyl allylation with the low-valent metals, such as $SnCl_2$,[2e] Sn,[2f] $MnCl_2$-$LiAlH_4$,[2i] $CrCl_3$–$LiAlH_4$,[2j] and VCl_3–$LiAlH_4$,[6] instead of Zn, were not found to occur significantly under the same conditions. It is noteworthy that the reaction intermediate apparently has the opposite charge to the conventional π-allylpalladium compounds.[7]

The results of the allylation of aldehydes by various allylic acetates with $Pd(PPh_3)_4$–Zn are summarized in Table I. When 2 equiv of allylic acetates were used, the

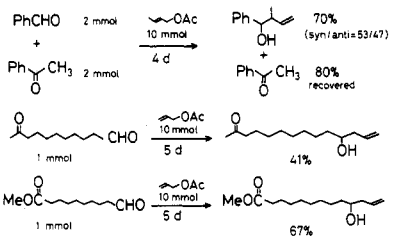
Scheme II



Scheme III



Scheme IV



(1) For review articles, see: (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357.

(2) (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, 1. (b) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (c) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. (d) Luche, J.-L.; Damiano, J.-C. *J. Am. Chem. Soc.* **1980**, *102*, 7926. (e) Mukaiyama, T.; Harada, T.; Shoda, S. *Chem. Lett.* **1980**, 1507. (f) Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 1527. (g) Yamamoto, Y.; Maruyama, K. *Tetrahedron Lett.* **1981**, *22*, 2895. (h) Sato, F.; Iida, K.; Iijima, S.; Morita, H.; Sato, M. *J. Chem. Soc., Chem. Commun.* **1981**, 1140. (i) Souppe, J.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1982**, *23*, 3497. (j) Hiyama, T.; Obayashi, M.; Nakamura, A. *Organometallics* **1982**, *1*, 1249. (k) Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561. (l) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191. (m) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904. (n) Uneyama, K.; Kamaki, N.; Moriya, A.; Torii, S. *J. Org. Chem.* **1985**, *50*, 5396. (o) Petrier, C.; Einhorn, J.; Luche, J.-L. *Tetrahedron Lett.* **1985**, *26*, 1449. (p) Wada, M.; Akiba, K. *Tetrahedron Lett.* **1985**, *26*, 4211. (q) Tanaka, H.; Yamashita, S.; Hamatani, T.; Ikemoto, Y.; Torii, S. *Chem. Lett.* **1986**, 1611. (r) Uneyama, K.; Nanbu, H.; Torii, S. *Tetrahedron Lett.* **1986**, *27*, 2395.

(3) (a) Collum, D. B.; McDonald, J. H., III; Still, W. C. *J. Am. Chem. Soc.* **1980**, *102*, 2118. (b) Fujita, K.; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258. (c) Roush, W. R.; Adam. M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 3422. (d) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919.

(4) (a) For reaction with (allyloxy)benzimidazole, see: Yamaguchi, M.; Mukaiyama, T. *Chem. Lett.* **1980**, 993. (b) For reaction with allylic phosphate, see: Matsubara, S.; Wakamatsu, K.; Morizawa, Y.; Tsubouchi, N.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1196. (c) For reaction with allylic acetate, see: Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 1195.

(5) The carbonyl allylation was not further promoted by using a Zn–Cu couple instead of Zn under the same conditions.

(6) Ho, T.-L.; Olah, G. A. *Synthesis* **1977**, 170.

(7) (a) Trost, B. M.; Verhoeven, T. R. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, 1982; Vol. 8, p 802. (b) Hegedus, L. S. *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Ed.; Elsevier: Amsterdam, 1984; p 30. (c) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic: London, 1985; p 117. (d) Tsuji, J. *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Ed.; Wiley: New York, 1985; Vol. 3, p 163.

yields based on the aldehydes decreased compared to the yields when 5 equiv of the acetates were used. This decrease was because of palladium-catalyzed homocoupling of the acetates.[8] Aromatic and α,β-unsaturated aldehydes can be used in this Pd(0)–Zn system.[9] Further, the aldehyde regioselectively attacked the more substituted allylic position of the π-allylpalladium complex to give a single regioisomer (Scheme II and III).[10] Consequently, the carbonyl allylation exhibits slight diastereoselectivity (syn selectivity) except the cases of 1-phenyl-2-propenyl acetate and 3-phenyl-2-propenyl acetate. Ketones such as 4-*tert*-butylcyclohexanone and acetophenone did not react under the same conditions. As shown in Scheme IV, the allylation of an aldehyde was chemoselectively performed in the presence of a ketone group or an ester group.[2k,q]

Allylic acetates function as synthons of the corresponding allylic carbanions. However, the carbonyl allylation does not exhibit the high diastereoselectivity. Therefore, further investigation for enhancing the selectivity is in progress.

(8) Sasaoka, S.; Yamamoto, T.; Kinoshita, H.; Inomata, K.; Kotake, H. *Chem. Lett.* **1985**, 315.

(9) In this Pd(0)–Zn system, pinacol-type self-coupling products were not detected by thin-layer chromatography. In the Pd(0)–SmI_2 system, which is the only method using allylic acetates in the carbonyl allylation, aromatic and α,β-unsaturated aldehydes cause the pinacol-type self-coupling; see ref 4c.

(10) In the Pd(0)–SmI_2 system, the aldehyde causes the electrophilic attack at the less substituted allylic position; see ref 4c.

(11) For determination of the ratios of syn/anti isomers, see: Koreeda, M.; Tanaka, Y. *Chem. Lett.* **1982**, 1299.

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Unusual Cyclopropane-Containing Hapalindolinones from a Cultured Cyanobacterium

Summary: Two structurally unusual indolinones containing a spiro-fused cyclopropane and an isonitrile have been isolated from the cells of a cultured cyanobacterium.

Sir: In a search for inhibitors of arginine vasopressin binding, the unusual indolinones **1A** and **1B** have been isolated from the cells of a cultured cyanobacterium belonging to the genus *Fischerella* (ATCC 53558). The structures were elucidated by IR, NMR, and mass spectral analysis and the stereochemistry and absolute configuration of **1A** established with single-crystal X-ray diffraction analysis.

The producing culture was isolated and purified from an enrichment culture established by using a soil sample obtained from the Everglades, Florida. This cyanobacterium is filamentous and exhibits true branching and a complex developmental cycle. On the basis of its morphological characteristics, this culture appears to be a member of typological group V, as defined by Rippka et al.[1]

(1) Rippka, R.; Deruelles, J.; Waterbury, J. B.; Herdman, M.; Stanier, R. Y. *J. Gen. Microbiol.* **1979**, *111*, 1–66.

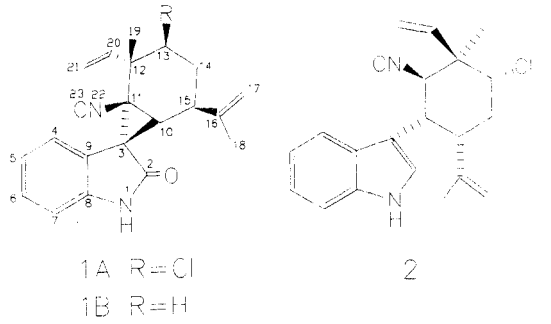

Figure 1.

Cultures were grown axenically in 1 L of BG-11 medium,[2] prepared by using 5 mM of HEPES–NaOH buffer, pH 8.5. Incubation was carried out in a 2800-mL Fernbach flask shaken at 100 rpm and 29 °C at a light intensity of 3500 lux. The headspace of the culture vessel was continuously flushed with humidified 5% (v/v) CO_2 in air at a flow rate of 200 mL/min. After 17 days incubation, the cells (~3.5 g wet w/L) were harvested.

Compounds **1A** and **1B** are related to the hapalindoles[3] and, in particular, hapalindole E (**2**),[4,5] which were also isolated from a cultured cyanobacterium, *Hapalosiphon fontinalis* (ATCC 39694).

Compound **1A** was isolated by MeOH extraction (3×) of the cells obtained from 1 L of the cyanobacterium culture. The MeOH extracts were filtered, combined, concentrated, and partitioned with CH_2Cl_2. The CH_2Cl_2 layer was concentrated and chromatographed on silica gel (CH_2Cl_2) to yield 18 mg of crystalline **1A** (92–96 °C dec) $[\alpha]^{25}_D$ −30°. Compound **1B** was further purified via Sephadex LH-20 (CH_2Cl_2/hexane/MeOH, 10:10:1) chromatography to yield 5 mg of a colorless oil.

Low resolution mass spectra of **1A** indicated the presence of a single Cl while high resolution analysis suggested the formula $C_{21}H_{21}N_2OCl$ (calcd 352.1342, found 352.1347).[6] Comparison showed that compound **1A** had an oxygen and one more unsaturation than hapalindole E (**2**) ($C_{21}H_{23}N_2Cl$). The IR spectrum of **1A** suggested the presence of an isonitrile, an -NH, and a carbonyl group with absorbances at 2125 cm^{-1}, 3420 cm^{-1}, and 1716 cm^{-1}, respectively (Figure 1).

The ^1H NMR data for **1A** (Table I) differed from hapalindole E (**2**) in the absence of signals for the protons on C2 and C11, an upfield shift of 1.3 ppm for the proton on C10, and a downfield shift of 1.3 ppm for the proton on C13. Also, only the proton on C15 was coupled to the proton on C10.

The absence of a proton on C2 and the presence of a carbonyl, as noted in the ^1H NMR and IR spectra, suggested that the indole in **2** was now an indolinone in **1A**. Also, the disappearance of the proton on C11 and the absence of an additional proton on C3, along with the knowledge that **1A** contained another unsaturation site,

(2) Rippka, R.; Waterbury, J. B.; Stanier, R. Y. *The Prokaryotes—A Handbook on Habitats, Isolation and Identification of Bacteria*; Springer-Verlag: New York, 1981; pp 212–220.

(3) Moore, R. E.; Cheuk, C.; Patterson, G. M. L. *J. Am. Chem. Soc.* **1984**, *106*, 6456–6457.

(4) Moore, R. E.; Patterson, G. M. L. Eur. Pat. Appl. 85 305 600.0, 1986.

(5) Moore, R. E.; Cheuk, C.; Yang, X. G.; Patterson, G. M. L.; Bonjouklian, R.; Smitka, T. A.; Mynderse, J. S.; Foster, R. S.; Jones, N. D.; Swartzendruber, J. K.; Deeter, J. B. *J. Org. Chem.* **1987**, *52*, 1036–1043.

(6) Mass spectra were obtained on a Finnigan Mat 212 mass spectrometer at 3 kV in the electron impact mode; high resolution data was obtained by using the peak match method with PFK (perfluorokerosene) as the internal standard.

(7) Gassman, P. G.; Gilbert, D. P.; Luh, T. *J. Org. Chem.* **1977**, *42*, 1340–1344.

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